

1. A process for preparing 5-( $\alpha$ -haloacetyl)-8-substituted oxy-(1*H*)-quinolin-2-ones comprising:
  - (a) reacting
    - (i) 8-hydroxy-(1*H*)-quinolin-2-one with an acylating agent and a Lewis acid to form 5-acetyl-8-hydroxy-(1*H*)-quinolin-2-one; or
    - (ii) 8-hydroxy-(1*H*)-quinolin-2-one with an acylating agent to form 8-acetoxy-(1*H*)-quinolin-2-one, and treating, in-situ, the 8-acetoxy-(1*H*)-quinolin-2-one with a Lewis acid to form 5-acetyl-8-hydroxy-(1*H*)-quinolin-2-one; or
    - (iii) 8-acetoxy-(1*H*)-quinolin-2-one with a Lewis acid to form 5-acetyl-8-hydroxy-(1*H*)-quinolin-2-one;
  - (b) reacting the 5-acetyl-8-hydroxy-(1*H*)-quinolin-2-one prepared in Step (a) with a compound having the Formula RL in the presence of a base and a solvent to form 5-acetyl-8-substituted oxy-(1*H*)-quinolin-2-one, wherein R is a protecting group and L is a leaving group; and
  - (c) reacting the 5-acetyl-8-substituted oxy-(1*H*)-quinolin-2-one with a halogenating agent in the presence of a solvent to form a 5-( $\alpha$ -haloacetyl)-8-substituted oxy-(1*H*)-quinolin-2-one.
2. A process according to Claim 1, wherein the acylating agent, which is preferably acetic anhydride or acetyl chloride, is present in an amount of from 1 molar equivalents to 1.5 molar equivalents, based on the molar equivalents of 8-hydroxy-(1*H*)-quinolin-2-one.
3. A process according to Claim 1 or 2, wherein the Lewis acid, which is preferably boron trifluoride, aluminium chloride or titanium tetrachloride, is present in an amount of from 3 molar equivalents to 5 molar equivalents, based on the molar equivalents of 8-hydroxy-(1*H*)-quinolin-2-one or on the molar equivalents of 8-acetoxy-(1*H*)-quinolin-2-one.
4. A process according to any one of Claims 1 to 3, wherein Step (a) is conducted in the presence of an ionic compound, wherein the ionic compound is either an alkaline halide

selected from the group consisting of sodium chloride, sodium bromide, lithium chloride and lithium bromide or an ionic liquid selected from the group consisting of an imidazolium salt, pyridium salt, ammonium salt, phosphonium salt and sulphonium salt.

5. A process according to any one of Claims 1 to 4, wherein the compound having the Formula RL is selected from the group consisting of  $\alpha$ -methylbenzyl bromide, methyl chloride, benzylchloride and benzylbromide.

6. A process according to any one of Claims 1 to 5, wherein the 5-acetyl-8-substituted oxy-(1H)-quinolin-2-one is 5-acetyl-8-benzyloxy-(1H)-quinolin-2-one.

7. A process according to any one of Claims 1 to 6, wherein the halogenating agent is selected from the group consisting of sodium bromate and hydrobromic acid, bromine, N-bromosuccinimide, N-chlorosuccinimide, iodine, chlorine, sulfuryl chloride, benzyltrimethylammoniumdichloro-iodate, copper chloride, pyridinium tribromide, tetraalkylammonium tribromide, iodine chloride, hydrochloric acid and an oxidating agent and combinations thereof.

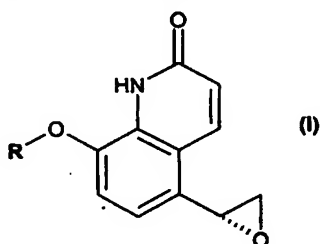
8. A process according to Claim 7, wherein the halogenating agent is benzyltrimethylammoniumdichloroiodate.

9. A process according to any one of Claims 1 to 8, wherein the 5-( $\alpha$ -haloacetyl)-8-substituted oxy-(1H)-quinolin-2-one is 5-( $\alpha$ -chloroacetyl)-8-benzyloxy-(1H)-quinolin-2-one.

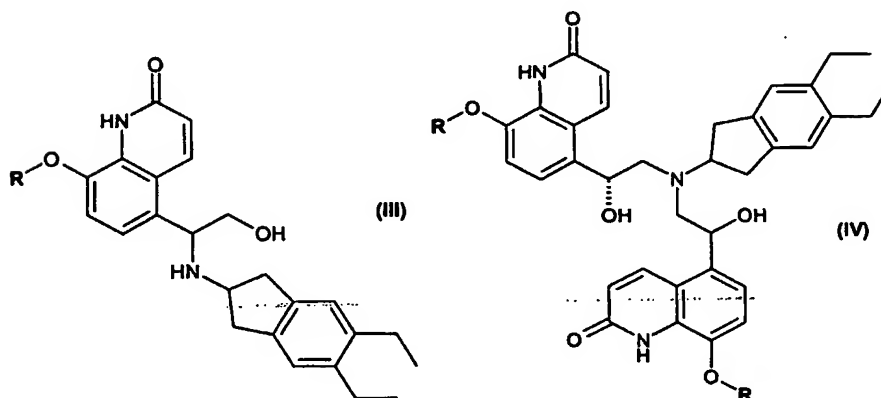
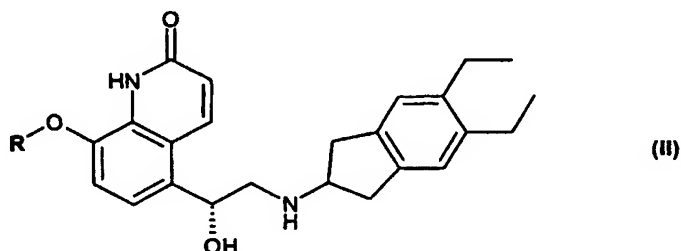
10. A process according to any one of Claims 1 to 9, wherein in Step (a) the solvent is selected from the group consisting of methylenechloride, 1,2-ethylene dichloride, chlorobenzene, *o*-dichloro-benzene, aliphatic C<sub>6</sub>-C<sub>12</sub>-hydrocarbons and combinations thereof; in Step (b) the solvent is selected from the group consisting of acetone, methyl isobutyl ketone, tetrahydrofuran, diisopropyl ether, 2-methoxyethyl ether, diethylene ether, methylenechloride, water and combinations thereof; and in Step (c) the solvent is selected from the group consisting of acetic acid, trifluoroacetic acid, propionic acid; ethyl acetate, isopropyl acetate, butyl acetate, toluene, benzene, tetrahydrofuran, diisopropyl ether, 2-methoxyethyl ether, diethylene ether, methylenechloride and combinations thereof.

11. A process according to any one of Claims 1 to 10, wherein in Step (a) the temperature is from 0 °C to 160 °C; in Step (b) the temperature is from 20 °C to 90 °C; and in Step (c) the temperature is from about 10 °C to about 160 °C.
12. A process for preparing 5-[(R)-2-(5,6-diethyl-indan-2-ylamino)-1-hydroxy-ethyl]-8-hydroxy-(1*H*)-quinolinone-2-one salts comprising:
- (a) reacting
- (i) 8-hydroxy-(1*H*)-quinolin-2-one with an acylating agent and a Lewis acid to form 5-acetyl-8-hydroxy-(1*H*)-quinolin-2-one; or
- (ii) 8-hydroxy-(1*H*)-quinolin-2-one with an acylating agent to form 8-acetoxy-(1*H*)-quinolin-2-one, and treating, in-situ, the 8-acetoxy-(1*H*)-quinolin-2-one with a Lewis acid to form 5-acetyl-8-hydroxy-(1*H*)-quinolin-2-one; or
- (iii) 8-acetoxy-(1*H*)-quinolin-2-one with a Lewis acid to form 5-acetyl-8-hydroxy-(1*H*)-quinolin-2-one;
- (b) reacting the 5-acetyl-8-hydroxy-(1*H*)-quinolin-2-one prepared in Step (i) with a compound having the Formula RL in the presence of a base and a solvent to form 5-acetyl-8-substituted oxy-(1*H*)-quinolin-2-one, wherein R is a protecting group and L is a leaving group;
- (c) reacting the 5-acetyl-8-substituted oxy-(1*H*)-quinolin-2-one with a halogenating agent in the presence of a solvent to form a 5-( $\alpha$ -haloacetyl)-8-substituted oxy-(1*H*)-quinolin-2-one;
- (d) reacting an 5-( $\alpha$ -haloacetyl)-8-substituted oxy-(1*H*)-quinolin-2-one with a reducing agent in the presence of a chiral catalyst to form 8-(substituted oxy)-5-((R)-2-halo-1-hydroxy-ethyl)-(1*H*)-quinolin-2-one;
- (e) treating the 8-(substituted oxy)-5-((R)-2-halo-1-hydroxy-ethyl)-(1*H*)-quinolin-2-one with a base in the presence of a solvent to form 8-(substituted oxy)-5-(R)-oxiranyl-(1*H*)-quinolin-2-one;

- (f) reacting the 8-substituted oxy-5-(R)-oxiranyl-(1*H*)-quinolin-2-one having Formula (I)

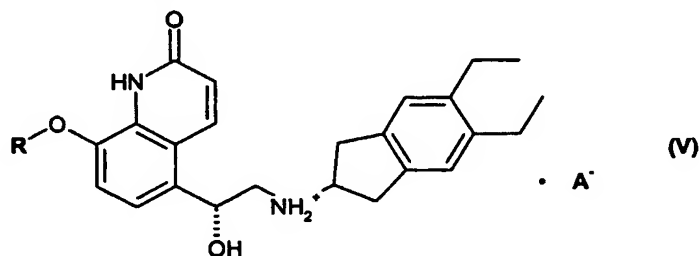


with 2-amino-(5-6-diethyl)-indan to form a reaction mixture containing compounds having Formulae (II), (III) and (IV)



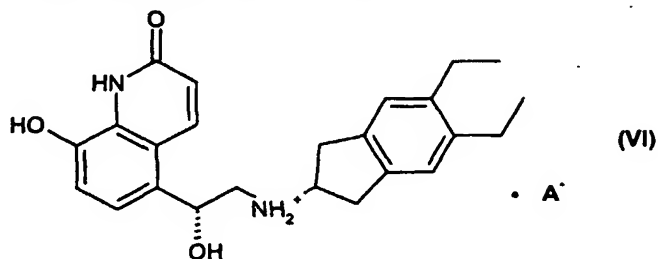
wherein R is a protecting group;

- (g) treating the reaction mixture prepared in Step (i) with an acid in the presence of a solvent to form a corresponding salt;
- (h) isolating and crystallizing a salt having Formula (V)



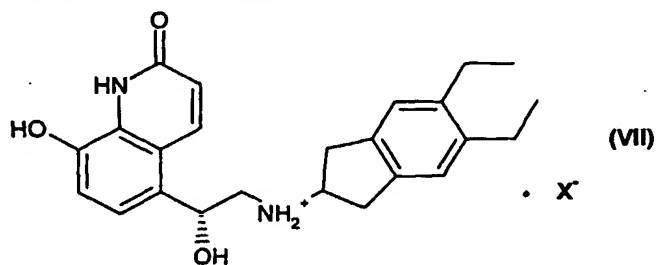
wherein R is a protecting group and A<sup>-</sup> is an anion;

- (i) removing the protecting group from the salt having Formula (V) in the presence of a solvent to form a salt having Formula (VI):



wherein  $A^-$  is an anion; and

- (j) treating the salt having Formula (VI) with an acid in the presence of a solvent to form 5-[(R)-2-(5,6-diethyl-indan-2-ylamino)-1-hydroxy-ethyl]-8-hydroxy-(1H)-quinolin-2-one salt having Formula (VII)



wherein  $X^-$  is an anion.